low dose ASA alone, the multivariate adjusted significance was 0.01. Conclusion: In a healthy population without known coronary disease, after controlling for major risk factors, the use of ASA and a statin alone remains significantly associated with lower levels of inflammation, and importantly the combination of both a statin and aspirin is a particularly strong independent predictor of lower levels of hs-CRP. These findings suggest that daily statin and aspirin therapy combined may be particularly potent in reducing inflammation in high risk individuals who have not yet had a clinical coronary event.

2:30 p.m.

847-3 Aspirin Resistance Is Associated With a Single Nucleotide Polymorphism in the P_2Y_1 ADP Receptor Gene

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Background: Lack of platelet aggregation response to aspirin resistance (AR) has been reported in 5-30% of patients. Using strict criteria for AR, we have shown a three fold increased risk of death, MI and CVA. The underlying mechanisms for the variable effect of aspirin remain unclear and are likely multi-factorial. Polymorphisms in platelet surface receptors may alter the response of platelets to pharmacologic agents and play a role in aspirin sensitivity.
Methods: We examined 7 candidate single nucleotide polymorphisms in the COX-1, COX-2, GPIIIa, and P_2Y_1(P2RY1) genes in 332 patients on aspirin with a history of MI from the Gene Quest 2 database. Aspirin resistance was assessed using optical aggregation in response to arachidonic acid and ADP. Aspirin sensitive (aggregation $\leq$20%) and resistant (>20%) subjects were compared using multiple logistic regression. DNA was genotyped using standard PCR techniques.
Results: In the study population, 235(71%) were classified as aspirin sensitive and 95(29%) were classified as aspirin resistant. Clinical comparisons between aspirin sensitive and aspirin resistant patients revealed a significant difference between the groups in age (63.3 y/68.4 y), HDL cholesterol (39 mg/dl/35.6 mg/dl), and incidence of diabetes (22%/37%). Using logistic regression analysis, patients with the P2RY1 C/T893 genotype displayed a statistically significant 3-fold higher risk of aspirin resistance over those with the P2RY1 C/C893 genotype. The risk of aspirin resistance remained even after adjusting for the above confounding variables: Adjusted OR 2.72 (95% C.I. 1.12, 6.57). Single nucleotide polymorphisms in other candidate genes were not associated with aspirin resistance.
Conclusions: There are demographic differences between aspirin sensitive and aspirin resistant patients which are in agreement with previous reports. After controlling for these variables, the P2RY1 C/T893 polymorphism is associated with decreased platelet responsiveness to aspirin. Polymorphisms in the P_2Y_1 receptor gene may provide a genetic link in the variable clinical responsiveness of patients to aspirin and requires confirmation and elucidation of the mechanism.

2:45 p.m.

847-4 Asymmetric Dimethylarginine and the Risk of Coronary Heart Disease: Relationship With Traditional Risk Factors as Assessed in the Multicenter CARDIAC Study

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Background. Asymmetric dimethylarginine (ADMA) is an endogenous inhibitor of NO synthase. In human subjects, its levels are related to endothelial dysfunction and the progression of carotid atherosclerosis. In patients with end-stage renal disease, ADMA is prospectively associated with the risk of major cardiovascular events and death.
It was the aim of the CARDIAC study (Coronary Artery Risk Determination investigating the Influence of ADMA Concentration) to assess the relationship between ADMA concentration and the risk for coronary heart disease (CHD) in a large population including subjects with a broad range of established coronary risk factors of both sexes and with normal renal function. We also studied the relationship between ADMA and traditional risk factors in risk determination.
Methods. 408 patients with established CHD and 408 controls matched for age and sex were enrolled. Besides traditional risk factors, plasma levels of ADMA and its biologically inactive regioisomer, symmetric dimethylarginine (SDMA), and L-arginine were determined.
Results. CHD patients had significantly higher ADMA plasma concentration than controls (median, 0.91 vs. 0.70 µmol/L; p<0.0001). ADMA was an independent predictive factor for the risk of CHD, whereas SDMA was not associated with CHD. ADMA levels significantly increased with increasing number of established cardiovascular risk factors present (p<0.01). The presence of hypertension was associated with significantly higher ADMA levels (median, 0.95 vs. 0.87 µmol/l; p<0.05), whereas hypercholesterolemia was associated with lower ADMA (0.85 vs. 1.03 µmol/l; p<0.05; probably due to the high rate of treated hypercholesterolemia), and diabetes mellitus had no significant effect on ADMA. Former smokers had higher ADMA than current smokers or non-smokers (1.16 vs. 0.70 and 0.88 µmol/l, respectively; p<0.01).
Conclusions. The present data show for a large group of subjects of both sexes and with a broad range of established coronary risk factors that ADMA is an independent marker of CHD. Thus, determination of ADMA may help to identify patients at risk for coronary events beyond currently established risk factors.

3:00 p.m.

847-5 Systolic Blood Pressure Measured Serially From Childhood to Adulthood Predicts Arterial Stiffness in Young Adults: The Bogalusa Heart Study

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Backgroud: Arterial stiffness is associated with cardiovascular risk factors and is an independent predictor of cardiovascular disease and events even after adjusting for other traditional risk factors. However, no data are available regarding the relationship of arterial stiffness in young adults to different risk factors measured in childhood, adulthood, or as a cumulative burden from childhood to adulthood.
Methods: The study sample included 839 young adults (72% whites, 44% males) aged 24 to 44 years who had at least four measurements of traditional risk factors including body mass index (BMI), systolic blood pressure, low- and high-density lipoprotein (LDL and HDL) cholesterols, and triglycerides since childhood. The average follow-up period was 26.5 years. Brachial to ankle pulse wave velocity (baPWV) by oscillometric method was used as a measure of arterial stiffness. Cumulative burden of risk factors since childhood was measured as area under the curve divided by follow-up years.
Results: Males vs females and black vs whites had higher levels of baPWV (P<0.001). Systolic blood pressure, BMI, and HDL cholesterol measured in childhood, all the risk factors measured in adulthood, and cumulative burdens of systolic blood pressure, triglycerides, BMI, and HDL cholesterol were significant risk factors for baPWV in young adults in univariate analyses. In multiple regression analyses, childhood systolic blood pressure, adulthood systolic blood pressure and triglycerides, and cumulative burdens of systolic blood pressure and triglycerides since childhood were significant and independent risk factors for baPWV in young adults.
Conclusion: These results indicate that among the traditional cardiovascular risk factors, systolic blood pressure measured either in childhood, adulthood, or as a cumulative burden since childhood is a consistent predictor of arterial stiffness in young adults, and underscores its importance in the process of arterial stiffening.

3:15 p.m.

847-6 Serum Inflammatory Markers Correlate With Hemoglobin Levels in Women Undergoing Evaluation for Suspected Ischemia: Results From the National Heart, Lung, and Blood Institute WISE Study

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Background: Serum inflammatory markers such as C-reactive protein have been shown to predict cardiovascular morbidity and mortality. Anemia is emerging as a risk factor for morbidity and mortality in patients presenting with acute myocardial infarction or heart failure, and other WISE data indicates that lower hemoglobin levels are significantly associated with worse cardiovascular outcomes. However, the relationship between serum inflammatory markers and hemoglobin levels in women presenting with chest pain is not known.
Methods: As part of the NHLBI-sponsored Women's Ischemia Syndrome Evaluation (WISE), we collected data including baseline hemoglobin level, high sensitivity C-reactive protein (CRP), IL-6, and TNF-alpha levels in 602 women referred for coronary angiography to evaluate suspected ischemia. We then compared the hemoglobin levels with serum inflammatory marker levels.
Results: Of the women enrolled, the mean age was 58.0 $\pm$ 11.7 yrs, and 35% had angiographic CAD stenoses of >50%, 26% had diabetes, 58% had hypertension, 54% had dyslipidemia, and 20% were current smokers. As hemoglobin levels increased, serum inflammatory marker levels including CRP (p=0.05), IL-6 (p=0.005), and TNF-alpha (p=0.009) decreased. A hemoglobin <12 g/dL was also associated with significantly higher levels of CRP (p=0.02), IL-6 (p<0.001), and TNF-alpha (p=0.006). After adjusting for waist/hip ratio, lipid levels, statin use, ACE-inhibitor use, aspirin or other antiplatelet medication use, and angiographic CAD, hemoglobin <12g/dL was associated with increased CRP (p=0.07), IL-6 (p< 0.01), TNF-alpha (p<0.01).
Conclusions: Serum inflammatory markers are inversely related to hemoglobin levels in this population of women evaluated for suspected ischemia. Underlying inflammation may contribute to both decreased hemoglobin levels and increased cardiovascular morbidity and mortality found in this population of women.